REMARKS

After entry of this amendment, claims 1-2, 4-5, 7-17 and 26-27 are pending. Claims 3, 6 and 18-25 have been cancelled without prejudice or disclaimer. New claims 26 and 27 have been added and find support *inter alia* in the original claims. Further support for newly added claim 26 is found in the specification at page 24, lines 15-18. New claim 27 finds further support in the specification at page 11, lines 14-18 and page 22, lines 9-11. The claims have been amended without prejudice and disclaimer to delete the non-elected subject matter, to better comply with the U.S. practice, and to address various points made in the Official Action. The amended claims find support *inter alia* in the original claims. Claim 1 finds further support in original claims 7-9 and in the specification at page 11, lines 13-14 and page 20, lines 24-27. Claim 5 finds further in the specification support at page 24, lines 15-18 and page 45, lines 14-15. No new matter has been added. New claims 26 and 27 are believed to be consistent with the restriction requirement.

Claim Objections

Claims were objected to for containing non-elected subject matter and various formality issues. The objections are believed to be rendered moot in view of the amendment. Applicants respectfully request withdrawal of the objections.

Rejections under 35 USC § 112, second paragraph

Claims 5 and 14-15 were rejected under 35 USC § 112, second paragraph, as being indefinite. Applicants respectfully disagree. However, in order to expedite prosecution, the claims have been amended without prejudice or disclaimer. The rejections are believed to be rendered moot.

Additionally, the Examiner rejects claim 5 for the recitation "negligible." Applicants strongly disagree. As stated in § 2173.02 of the M.P.E.P. "[t]he test for definiteness under 35 U.S.C. 112, second paragraph, is whether 'those skilled in the art would understand what is claimed **when the claim is read in light of the specification**.'" (M.P.E.P. § 2173.02, emphasis

added). If one skilled in the art is able to ascertain the meaning of the terms in light of the specification, 35 U.S.C. 112, second paragraph, is satisfied. See M.P.E.P. § 2173.02. The meaning of "essential enzymatic or biological activity of the enzymes" is provided in the specification at pages 24-25 (see page 24, line 34 through page 25, line 6). Furthermore, the specification at page 45 discusses in detail what it means by "negligibly reduced" essential enzymatic activity. See page 45, lines 14-19. Thus, it is clear to one skilled in the art what the recitation "negligibly reduced enzymatic activity of SEQ ID NO: 2" in claim 5 means. Accordingly, Applicants respectfully submit that the claims are clear when read in view of the specification, and therefore, satisfy the requirements under 35 USC § 112, second paragraph.

Reconsideration and withdrawal of the rejections is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph

Written Description Rejection

Claims 1-2, 4, and 7-17 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. Applicants respectfully disagree and traverse the rejections for the following reasons.

Applicants disagree with the standard for written description asserted by the Examiner on pages 8 and 9 of the Office Action, which the Examiner acknowledged was "paraphrased" from "Enzo Biochem The Examiner alleges that Applicants to meet the Written Description requirement "must (1) fully describe at least one species of the claimed genus sufficient to represent the genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these." (Emphasis added).

Rather the Federal Circuit in *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 964 (Fed. Cir. 2002) citing to the "Guidelines for Examination of Patent Applications Under the 35

U.S.C.S. § 112, para. 1 "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (January 5, 2001)" and agreeing with the Patent Office's standard, stated that "the United States Patent and Trademark Office has determined that the written description requirement **can** be met by showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, i.e., complete **or partial** structure, other physical and/or chemical properties, functional characteristics when coupled with a known **or** disclosed correlation between function and structure, **or** some combination of such characteristics." (Emphasis added). Furthermore, the Patent Office's own standard under the Guidelines referred to above by the Court is different than that stated by the Examiner. As indicated in the Guidelines, the written description requirement for a claimed genus can be satisfied in a number of **alternative** ways, such as through sufficient description of a representative number of species by actual reduction to practice, by disclosure of relevant identifying characteristics, by functional characteristics coupled with known or disclosed correlation between function and structure, or by a combination of such identifying characteristics. The Examiner is requiring a different standard than the standard set forth by the Court of Appeal for the Federal Circuit and by the Patent Office. Furthermore, in *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997) cited by the Examiner, the Federal Circuit held that a "description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs..."

Under the correct standard, Applicants submit that the specification provide adequate written description for the following reasons. The specification provides at least three actual nucleic acids coding for threonine-degrading proteins (SEQ ID NO: 1, 13, and 15) and eleven actual amino acid sequences of threonine-degrading proteins (SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 14, and 16). Furthermore, the specification describes several sequences identified by GenBank Accession number with threonine-degrading activity at pages 16 and 17 which can be used in the method of the invention. At least fourteen actual sequences is clearly a "representative" number of species of the genus and the Examiner has not provided reasons why it is not. See also *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971); MPEP § 2163.04 (written description under 35 U.S.C. § 112, first paragraph, is presumed to be adequate, unless or until

sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption).

The Examiner cites to *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916 (Fed. Cir. 2004), for written description of methods of using products. The court in *University of Rochester* held that because the patent is suit did "not disclose any compounds that can be used in its claimed methods" written description was not adequate. In contrast, the present specification discloses at least fourteen actual sequences relating to threonine-degrading proteins of the present claims. Given that at least fourteen actual sequences are disclosed in the present specification rather than none, *University of Rochester* is not relevant to the present application.

The Examiner also alleges that the specification discloses the structure of only a single representative species of the genus (i.e. SEQ ID NO: 1) and does not contain any disclosure of the structures of all mutants or variants of any threonine-degrading enzyme (see Office Action page 9). Applicants respectfully disagree. As explained above, the present specification discloses at least fourteen actual sequences related to the elected subject matter of the present claims. Additionally, the specification shows in Examples 7-8 and 13 assays for determining activity and experiments showing activity. Because each embodiment need not be disclosed (see *In re Angstadt*), the specification provides a representative number of sequences under the standard of *Regents v. Lilly*. See *In re Angstadt*, 537 F.2d 498 (CCPA 1976) (holding that there has never been a requirement that every species encompassed by a claim must be disclosed or exemplified in a working example). Additionally, the specification discloses a common structure for the threonine aldolases and a common structure for the lysine decarboxylases (see for example Figures 1 and 2). Therefore, the representative species described here provide identifiable structural and functional characteristics of the genus claimed.

The Examiner has referred Applicants to the revised Guidelines for Written Description (see Office Action page 10). Example 18 of the "Synopsis of Application of Written Description Guidelines" is particularly relevant, since the claims of the present elected invention are drawn to methods and not to polynucleotides. The claims in Example 18 of the Guidelines relate to a method of producing a protein and are drawn to a genus, *i.e.* any of a number of methods that can

be used for expressing protein in mitochondria of the organism. Furthermore the recitation of a specific nucleic acid was not essential to the method. There was actual reduction to practice of a single embodiment, and there was no substantial variation within the claimed genus because there are a limited number of ways to practice the process steps.

Similar to Example 18, the present specification describes production of amino acids methionine, homoserine and lysine by introducing into an organism a polynucleotide comprising a nucleic acid sequence encoding a threonine-degrading protein, expressing the polynucleotide and harvesting the transgenic organism or obtaining amino acids. The specification also describes several sequences which encode threonine-degrading proteins and several sequences of threonine-degrading proteins. Morevover, the present specification describes an embodiment of the method in which a nucleic acid is transformed into microorganisms or plants. Additionally, as in Example 18 of the Guidelines, the present specification provides an actual reduction to practice of the method as shown in Examples 10-13. In Examples 10-13, a construct comprising a nucleic acid encoding a threonine-degrading protein was introduced into plants and the desired production of amino acids resulted. That process is the same irrespective of the selection of polynucleotide sequences encoding the threonine-degrading protein. As in Example 18 of the Guidelines, the present claims are adequately described.

Therefore, the specification provides for written description not only of a representative number of species by actual sequences, but also by disclosure of identifiable structural and functional characteristics. Thus, the specification meets the applicable test for adequate written description under both alternatives. Reconsideration and withdrawal of the rejection is respectfully requested.

Enablement Rejection

Claims 1-2, 4-5 and 7-17 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking an enabling disclosure. Applicants respectfully disagree and traverse the rejections. However, to expedite prosecution, the claims have been amended without prejudice

or disclaimer to recite the process with more clarity. Applicants respectfully request reconsideration in light of the amendment and for the following reasons.

First, the elected claims are directed to methods and not to the sequences themselves; thus, working examples for a specific sequence should not required. There has never been a requirement that every species encompassed by a claim must be disclosed or exemplified in a working example. *In re Angstadt*, 537 F.2d 498 (CCPA 1976).

As mentioned above, the specification provides detailed description and guidance regarding at least three actual nucleic acids coding for threonine-degrading proteins (SEQ ID NO: 1, 13, and 15) and eleven actual amino acid sequences of threonine-degrading proteins (SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 14, and 16), not one as alleged by the Examiner. Furthermore, the specification describes several sequences identified by GenBank Accession number with threonine-degrading activity at pages 16 and 17 which can be used in the method of the invention. Additionally, the specification discloses a common structure for the threonine aldolases and a common structure for the lysine decarboxylases (see for example Figures 1 and 2). The specification shows in Examples 7-9 and 13 experiments showing activity and assays for determining activity.

The Examiner acknowledges that methods of generating or isolating variants of polypeptides are well known in the art (see Office Action page 15). The specification additionally provides detailed guidance on how to identify variants of the sequences (for example, see page 24, lines 7-33, page 25, lines 15-25, page 41 line 1 through page 45 line 31) as well as how to test in routine assays for activity (see Examples 7-9 and 13) which is also well known to those skilled in the art as described in the specification (see Examples 7-9 and 13). For example, the specification in Example 10 describes cloning of SEQ ID NO: 1 with the use of primers as well as the use of this method for the other sequences of the invention (see page 60, lines 25-26). Example 11 describes in detail the production of transgenic plants expressing SEQ ID NO: 1 as well as the other sequences of the invention, *i.e.*, "[t]he other sequences used in the process were also expressed in plants analogously." (see page 63, line 14). Example 12 describes cultivation of plants for bioanalytical investigations which is applicable to plants

having the further sequences used in the process (see page 64, lines 10-11). Example 13 describes in detail metabolic analysis of transformed plants with results of the method. This detailed guidance and exemplification is applicable for any of the sequences used in the process.

As stated in *Ex parte Jackson*, under the applicable law, the test for "undue experimentation" is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. *Ex parte Jackson*, 217 USPQ 804, 807 (1982). Additionally, a patent need not disclose what is well known to those skilled in the art and preferably omits that which is well known to those skilled and already available to the public. *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991). In the present case, the specification provides detailed guidance and teaches in the Examples, as explained above, the types of routine assay which are employed to confirm activity and additionally a working example showing activity.

The Examiner alleges that a process comprising introducing a nucleic acid sequence obtained owing to the degeneracy of the genetic code of SEQ ID NO: 1 is not enabled. Applicants strongly disagree. As explained in Example 11 of the above referenced Patent Office Guidelines, the Patent Office states that "a person of skill in the art could readily envision all DNAs degenerate to SEQ ID NO: 1 by using a genetic code table." If one of skill in the art can envision all the DNAs degenerate to SEQ ID NO: 1, it is clear that it is well within their skill to make such DNAs, which is additionally routine for anyone of skill in the art.

In view of the detailed description, guidance, working examples, and high level of skill, the specification enables the full scope of the present claims without undue experimentation. On these facts, an analysis under *In re Wands* supports enablement. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (routine screening of hybridomas was not "undue experimentation;" the involved experimentation can be considerable, so long as "routine "). Reconsideration and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. § 102

The Examiner rejects claims 1-2, 5, 7, 10, and 14-16 under 35 U.S.C. 102(b) as being anticipated by Monschau *et al.* (hereinafter "Monschau"). Applicants respectfully disagree and traverse the rejection. However in order to expedite

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegall Bros., Inc. v. Union Oil Co.*, 814 F.2d 628, 631 (Fed. Cir. 1987). "[T]o hold that a prior art reference anticipates a claim, the Board must expressly find that every limitation in the claim was identically shown in the single reference." *Gechter v. Davidson*, 116 F.3d 1454, 1460 (Fed. Cir. 1997).

The Examiner alleges that Monschau teaches a method of producing L-amino acid glycine in a fungal strain *Ashbya gossypii* comprising and overexpressing a gene encoding threonine aldolase from *S. cerevisiae*. Applicants respectfully disagree with the Examiner's characterization. Monschau rather teaches riboflavin production in *A. gossypii* by enhancing the biosynthesis of the riboflavin precursor glycine through overexpression of the GLY1 gene from *A. gossypii*. The experiments described in Monschau resulted in increased riboflavin but only in the presence of threonine. Monschau does not teach a gene encoding threonine aldolase from *S. cerevisiae* but rather teaches isolation of an *A. gossypii* GLY1 gene and overexpression of this gene in the same fungal strain *A. gossypii* from which it was isolated (see Monschau abstract).

Nevertheless, in order to expedite prosecution, the claims have been amended without disclaimer or prejudice. As recited in the specification and in the claims, the present invention provides a method for the production of methionine, homoserine and lysine in transgenic organisms by introducing and expressing a nucleic acid encoding a threonine-degrading protein and harvesting the transgenic organism or obtaining one or more of the amino acids. Monschau does not teach or describe that the GLY1 gene influences the production of methionine, homoserine and lysine in transgenic organisms and thus does not teach harvesting transgenic organisms or obtaining these amino acids.

Because Monschau does not teach every limitation of the claims, Monschau does not anticipate the claims as amended. Reconsideration and withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. § 103

Claim 11 is rejected as being obvious under 35 U.S.C. § 103(a) over Monschau. Applicants respectfully traverse and urge reconsideration of the rejection for the following reasons.

To support a prima facie conclusion of obviousness, the prior art must disclose or suggest all the limitations of the claimed invention. See *In re Lowry*, 32 F.3d 1579, 1582 (Fed. Cir. 1994).

The Examiner contends that all microorganisms including filamentous fungus inherently produce L-amino acids including methionine, homoserine or lysine. Applicants respectfully disagree. It has been held that the mere fact that a certain thing may result from a given set of circumstances is not sufficient to establish inherency, that which may be inherent is not necessarily known, and that obviousness cannot be predicated on what is unknown, even if the inherency of a certain feature is later established. *In re Rijckaert* , 9 F.3d 1531, 1534 (Fed. Cir. 1993); see also MPEP § 2141.02 V. Similarly here, Monschau does not teach, suggest, or reveal that the GLY1 gene influences the production of methionine, homoserine and lysine in transgenic organisms. Absence such teaching or suggestion in the art, it would not have been obvious to use a threonine-degrading gene in a process for production of methionine, homoserine and/or lysine in transgenic organisms with a reasonable expectation of success that a threonine-degrading gene when expressed would produce methionine, homoserine and/or lysine.

Claims 12 and 13 rejected as being obvious under 35 U.S.C. § 103(a) over Monschau and in further view of Castigioni *et al* (hereinafter "Castigioni"). Applicants respectfully traverse and urge reconsideration of the rejection for the following reasons.

As explained above Monschau does not teach or suggest the production of methionine, homoserine and lysine in transgenic organisms. The Examiner relies on Castigioni for teaching plants transformed with a gene which increases glycine-betaine. Castigioni thus does not remedy the deficiency of Monschau. Because Monschau and Castigioni, alone or in combination, do not disclose or teach all the limitations of the present claims, Monschau and Castigioni do not render the claims obvious.

Additionally, a certified copy of the English language translation of the priority document is in preparation and will be submitted as soon as available if necessary. Accordingly, Castigioni is an applicable reference.

Furthermore, claims 11, 12 and 13, the only claims rejected for obviousness are dependent claims. In *In re Fine*, 837 F.2d 1071, 1076 (Fed. Cir. 1988), the court held that if an independent claim is nonobvious then any claim dependent therefrom is nonobvious. Because the independent claims are not part of the obviousness rejection, then the claims dependent therefrom are likewise nonobvious.

Reconsideration and withdrawal of the obviousness rejection is respectfully requested.

CONCLUSION

For at least the above reasons, Applicants respectfully request withdrawal of the rejections and allowance of the claims.

Accompanying this response is a petition for a three-month extension of time to and including March 7, 2008 with the required fee authorization. No further fee is believed due.

However, if an additional fee is due, the Director is authorized to charge our Deposit Account No. 03-2775, under Order No. 13195-00006-US from which the undersigned is authorized to draw.

Respectfully submitted,

By Roberte Makowski

Roberte M. D. Makowski, Ph.D.
Registration No.: 55,421
CONNOLLY BOVE LODGE & HUTZ LLP
Correspondence Customer Number: 23416
1007 North Orange Street, P.O. Box 2207
Wilmington, Delaware 19899
(302) 658-9141
(302) 658-5614 (Fax)
Attorney for Applicants

563259_1